EXHIBIT 14

Concise Communications

Nosocomial Pertussis Outbreak Among Adult Patients and Healthcare Workers

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ABSTRACT

We describe a pertussis outbreak among adult patients in a French general hospital following transmission from a healthcare worker. This index case transmitted pertussis to other healthcare workers, who, in turn, contaminated other staff and two immunosuppressed patients. This raises questions about infection control (*Infect Control Hosp Epidemiol* 2004;25:995-997).

Pertussis, a respiratory disease caused by *Bordetella pertussis*, can be prevented by vaccination. However, various studies, including national French studies, have shown a resurgence of this disease, with a change in its epidemiologic pattern in highly vaccinated populations.[1] Transmission is now observed from adults or adolescents to infants, who are susceptible to severe disease and potentially death. Healthcare workers (HCWs) in pediatric units are known to be at risk of infection, and numerous pertussis outbreaks have been reported in such units.[2] In this article, we describe the investigation of a pertussis outbreak among adult patients in a French general hospital following transmission of the infection through HCWs and adult patients.

METHODS

This investigation was performed in a general hospital (2,100 employees and 600 beds) located in the suburbs of Paris, France, after three cases of pertussis were confirmed among HCWs. There was no concurrent community outbreak. The nosocomial infection committee of the hospital arranged for all coughing subjects (HCWs and hospitalized patients) to be screened for the disease. Patients hospitalized on wards where HCWs were infected were eligible for this study if they developed a cough during their stay in the hospital or if they had a known chronic cough that changed in nature (spasmodic, nocturnal cough, or vomiting). Potential cases were identified by providing information about the outbreak to all employees during meetings and via the hospital intranet. We then questioned and examined all coughing subjects (pertussis vaccinations or disease history, medical history, physical examination, and chest x-ray) and performed pertussis diagnostic tests. These tests included amplification of the pertussis toxin (PT) promoter by polymerase chain reaction (PCR) performed on expectorations or nasopharyngeal aspirates obtained during the first examination[3] and measurement of anti-PT IgG using a previously described enzyme-linked immunosorbent assay (ELISA) method.[3] Culture was not performed because of its low sensitivity in adults.

Coughing subjects (HCWs and hospitalized patients) were divided into two groups. The first group (confirmed cases) contained subjects who had a positive result on PCR or an anti-PT IgG antibody titer higher than 100 ELISA units (EU)/mL, according to the definition of De Melker et al., based on one serum sample.[1,4] The second group (noncases) consisted of subjects with a negative or an unavailable result on PCR and an anti-PT IgG antibody titer lower than 100 EU/mL.

After confirmation of the first cases, most of the coughing employees were examined and treated with either spiramycin or azithromycin[5] for 5 days and given sick leave. All employees who were significantly exposed to or in contact with confirmed cases were given prophylactic azithromycin treatment for 5 days. Significant exposure consisted of at least 10 minutes of face-to-face contact or more than 1 hour spent in the room of a patient who had a confirmed case of pertussis.[2] Hospitalized patients with suspected and confirmed pertussis were accommodated in a single room. This decision was made to stop transmission of the disease to the hospital's obstetrics department, pediatric department, and several departments with immunocompromised patients. Surveillance lasted from November 17, 2000, until March 31, 2001, the end of the epidemic.

RESULTS

Eighty-nine subjects with a cough were examined: 77 HCWs (9 men and 68 women) and 12 hospitalized patients (5 males and 7 females). The mean ages of these subjects were 39.1 ± 13.2 years and 40.2 ± 14.2 years, respectively. Nine patients were hospitalized in the pneumology department, one in the obstetrics department, and two in the pediatric department (ages, 14.5 and 19 years). Five of the 12 patients were immunosuppressed (four patients with bronchopulmonary cancer receiving chemotherapy and one patient infected with human immunodeficiency virus).

Seventeen subjects (19%), all treated with macrolides, were classified as confirmed cases (Table). Fifteen of these subjects had a PT IgG titer higher than 100 EU/mL. Two subjects had a positive result on PCR and a PT IgG titer lower than 100 EU/mL, but one (patient 1) was immunocompromised. A second serum sample,

TABLE
DESCRIPTION OF THE 17 SUBJECTS WITH PERTUSSIS

Cough Beginning	Subject	Gender	Age (y)	Vaccinated	Duration of Cough at Diagnosis (d)	IgG Pertussis Toxin 1* (EU/mL)	IgG Pertussis Toxin 2† (EU/mL)	PCR
10/12/00	HCW 16 (NO)	F	51	-	60	670	680	-
10/31/00	HCW 5 (NO)	F	56	-	25	960	700	ND
11/3/00	HCW 2 (NO)	F	47	-	14	1,470	850	ND
11/7/00	HCW 6 (NO)	M	49	-	21	57	ND	+
11/18/00	HCW 8 (PhS)	F	22	+	25	9,760	ND	ND
11/23/00	HCW 14 (S)	F	47	-	15	1,250	960	ND
11/23/00	HCW 15 (S)	F	27	+	15	180	200	ND
12/1/00	HCW 21 (N)	F	42	-	12	176	194	-
12/1/00	HCW 30 (N)	F	37	+	15	196	204	ND
12/2/00	HCW 20 (N)	F	37	-	11	205	140	-
12/4/00	HCW 11 (N)	F	22	+	4	59	1,280	+
12/10/00	HCW 23 (N)	F	24	+	4	148	ND	ND
12/15/00	HCW 25 (St)	M	40	-	3	344	ND	-
12/26/00	Patient 1	M	62	-	14	19	16	+
2/22/01	Patient 2	F	14½	+	21	538	ND	+
3/2/01	HCW 99 (Ph)	F	45	-	25	1,540	ND	ND
3/16/01	HCW 100 (Ph)	M	40	-	21	200	ND	ND

PCR = polymerase chain reaction; HCW = healthcare worker; NO = nurse officer; N = nurse; Ph = physician; PhS = student physician; S = secretary; St = stretcher bearer; EU = enzyme-linked immunosorbent assay unit; ND = not done.
*Anti-pertussis toxin IgG measured in the first serum sample collected.
†Anti-pertussis toxin IgG measured in the second serum sample, which was collected 1 month after the first one.

collected 1 month after the first one, was obtained from 10 of the 17 patients with confirmed cases. However, only one more case was confirmed (HCW 11) by serology based on the analysis of two serum samples. This case had already been confirmed by PCR. Therefore, all of these data were in favor of the use of PCR or serology based on one serum sample for biological diagnosis of pertussis in adults.

HCW 6, a nurse officer who began coughing on November 7, was the first case confirmed by PCR (Table). The index case was HCW 16, who began coughing on October 12. This 51-year-old nurse officer was not vaccinated and had been coughing for 60 days at the time of diagnosis, despite multiple antibiotics. She was in contact, outside the hospital, with the mother of a newborn who was hospitalized for pertussis. As a result of weekly meetings, she contaminated three colleagues, who began to cough on October 31 (HCW 5), November 3 (HCW 2), and November 7 (HCW 6). A nurse (HCW 11) working on different wards of the hospital and a stretcher bearer (HCW 25), whose job entailed moving patients around the hospital, were involved in this epidemic. HCWs from seven departments were contaminated, with five major disease reservoirs: the physiotherapy, pediatrics, pneumology, and two internal medicine departments.

Two patients were confirmed to have pertussis. Both had already been in the hospital for longer than the incubation period of pertussis when they started coughing and neither had been visited by individuals with possible signs of pertussis infection. Both were in contact with infected HCWs and immunocompromised individuals. The first patient (patient 1) was a 62-year-old man with bronchopulmonary cancer and bone marrow metastasis who was undergoing chemotherapy. He initially had a new characteristic cough: post-tussive vomiting, post-tussive inspiratory effort, and sleep disturbed by cough without new opacity being found on chest x-rays. He then developed fainting episodes with cranial traumatism following a spasmodic cough. He required stitches and hospitalization for surveillance and diagnosis. The second hospitalized patient (patient 2) with confirmed nosocomial pertussis was a 14½-year-old girl infected with human immunodeficiency virus who had been correctly vaccinated in infancy. She had no opportunistic infection, but her CD4 count was only 191 cells/mm^3 and she had a viral load of 140,000 copies/mL despite antiretroviral treatment. The infection was diagnosed only after she had been coughing for 21 days.

Seventy-two subjects (81%) were classified as noncases. Among them, 87% were treated with macrolides.

Cases were compared with noncases for age using the Student's *t* test and for qualitative data using the chi-square test. Because the distribution of the duration of cough was not normal, this variable was expressed as median and range, and the analysis was performed using the Mann–Whitney *U* test. *P* values of less than .05 were

considered significant. Variables found to be significant on univariate analysis were included in a stepwise logistic regression model. The Statistica software package (version 3.1; StatSoft France, Maisons-Alfort, France) was used for analysis.

Mean age and prior contact with *B. pertussis* (by vaccination or infection) did not differ between confirmed cases and noncases (data not shown). Some clinical symptoms, such as coughing for more than 10 days at the time of diagnosis, productive cough, awakenings due to coughing, post-tussive vomiting, and post-tussive inspiratory effort, differed significantly between the two groups ($P < .05$), whereas coryza symptoms, fever, and spasmodic cough did not ($P > .05$) (data not shown). Eighty subjects were treated with macrolides, but no statistical test was performed because we decided to treat every coughing subject during this epidemic. Only four HCWs with confirmed pertussis did not stop working; their own general practitioners had prescribed macrolides for at least 5 days before the consultation, meaning that they were considered to no longer be contagious. To stop transmission, we decided to remove some of the HCWs from the hospital because of their cough. On multivariate analysis, coughing for more than 10 days at the time of diagnosis, productive cough, awakenings due to coughing, post-tussive vomiting, and post-tussive inspiratory effort remained significantly associated with confirmed cases (data not shown).

DISCUSSION

We have described the transmission of *B. pertussis* in a general hospital. Nosocomial outbreaks usually start following the admission of an infant with a cough or pneumonia due to pertussis or after the introduction of pertussis into a pediatric hospital from adult visitors.[1] The only instances in which HCWs have been reported to be affected have occurred in pediatric hospitals[1,2,6] or in residential facilities for the developmentally disabled.[1,7,8] We have reported the spread of *B. pertussis*, which did not originate in the pediatric department, in a general hospital. We suspected that the bacterium was transmitted from HCWs to patients. The fact that none of the individuals living in the same households as the patients coughed before them and that patients were in contact with infected HCWs during the incubation period strongly suggests nosocomial infection. The two patients with confirmed infection coughed for more than 14 days and were immunocompromised. Pertussis infection in patients with human immunodeficiency virus[9] or bronchopulmonary cancer has rarely been described.[10]

A HCW transmitted pertussis to other HCWs, who, in turn, transmitted it to other staff members and to patients. Eighty-nine adults with cough were examined; 80 were treated with macrolides and 40 were absent from work for 5 days. The economic burden of such an epidemic is currently being investigated.[11] Outbreaks among adults, including HCWs, provide support for a policy of booster vaccinations.

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Should Electronic Faucets Be Recommended in Hospitals?

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ABSTRACT

Microbiological examinations of electronic faucets newly installed in a hospital kitchen revealed high bacteria counts and *Pseudomonas aeruginosa* during a 6-month period of observation. Our data suggest that the use of electronic faucets poses a potential risk for nosocomial infection in high-risk areas of hospitals (*Infect Control Hosp Epidemiol* 2004;25:997-1000).

TABLE 1
WATER CULTURE RESULTS AFTER VARIOUS INTERVENTIONS

Period	Intervention	Study Day	No. of Samples	Exceeded Reference Values of Bacteria Counts		Detection of		
				CFU/mL at 22°C	CFU/mL at 36°C	Fecal Coliform Bacteria	*Pseudomonas*	Other Nonfermentative Bacteria
A	EFs installed	0	42	41 (98%)	40 (95%)	1 (2%)	4 (10%)	3 (7%)
B	Flushing	6	16	2 (12%)	1 (6%)	0	0	0
C	No intervention	62	27	26 (96%)	27 (100%)	0	0	0
D	Flushing	102	27	10 (37%)	5 (19%)	0	4 (15%)	0
E	Check valve installed	118	22	9 (41%)	8 (36%)	0	3 (14%)	0
F	Chlorination	153	7	6 (86%)	1 (14%)	1 (14%)	0	0
G	Change of faucet aerators	168	3	3 (100%)	3 (100%)	0	0	0

EFs = electronic faucets; CFU = colony-forming units.

Conventional hand-operated faucets were replaced with electronically operated ones in different locations of many institutions. These electronically operated faucets work without a handle. They were installed in commercial and public areas. Due to their technical construction, these systems can save water and therefore money. Their nontouch technique of operation also prevents contamination by hand contact. Due to this advantage, these devices have been more frequently installed in hospitals to prevent cross-contamination or recontamination. However, some authors have mentioned that problems can occur with these devices in hospitals.[1-3]

The Medical School Hannover is a 1,333-bed, tertiary-care, university teaching hospital with a kitchen that serves patients, personnel, and students. After renovation of this kitchen, we had the opportunity to examine newly installed electronic faucets. Due to initial problems for a period of 6 months, several measures for improving water quality were instituted and the results were investigated by the technical department.

METHODS

Twenty-seven electronic faucets (Moratronic, MORA GmbH, Norderstedt, Germany) newly installed in the renovated kitchen of the hospital were examined. These faucets worked by a nontouch technique with a sensor-operated system without a handle. The microbiological examinations were performed according to the German drinking water regulation about quality of water for human consumption based on guideline 98/93 of the European Union.[4] Samples were collected aseptically in sterile 500-mL glass bottles containing sodium thiosulfate to neutralize chlorine disinfectants. The bacteriologic check was immediately performed in a microbiological laboratory. In addition, cetrimide agar, a selective growth medium, was used to detect *Pseudomonas aeruginosa*. According to the German drinking water regulation previously mentioned, limit values exist for fecal coliform bacteria and *Escherichia coli*. These bacteria should not be detectable in 100 mL of potable water. The reference value for water that can be declared potable is less than 100 colony-forming units (CFU)/mL. Any bacteria counts exceeding this and the detection of indicator organisms such as fecal coliform bacteria, *E. coli*, or *P. aeruginosa* were considered evidence of contamination and thus rendered unacceptable.

To control the quality of the tap water throughout the entire research period, additional samples were taken from conventional manual faucets in the kitchen that had the same water supply system.

RESULTS

Due to unacceptable results, the examinations were repeated during a period of 168 days. Altogether, 144 analyses were conducted. Of these, 105 (73%) of the water samples did not comply with the German drinking water regulation. The analyses of the individual examinations are detailed in Table 1. In the first period (period A) before the kitchen was opened, almost 98% of the water samples that were taken three times within a period of 10 days showed bacteria counts greater than the reference values. *P. aeruginosa* and other nonfermentative gram-negative bacteria were also detected as well as fecal coliform bacteria. The electronic faucets were flushed for 48 hours to eliminate this bacterial contamination. After this measure, only 12% of the water samples showed bacteria counts greater than the reference values and none showed fecal coliform bacteria, *P. aeruginosa*, or other gram-negative nonfermentative bacteria (Table 1, period B).

TABLE 2
SUMMARY OF PUBLISHED STUDIES ABOUT ELECTRONIC FAUCETS

Study	Location	Type of Investigation	No. of EFs	Exceeded Reference Values of Bacteria Counts*	*Pseudomonas aeruginosa* Growth	Comments
Assadian et al.[9]	Hospital	Case–control study	18	Not mentioned	0%	
Halabi et al.[1]	Hospital	Cross-sectional study	10	60%	100%	In comparison with 10 conventional without temperature selection
Hargreaves et al.[2]	Surgical critical care unit	Cross-sectional study	34 brand A	32%†, 52%† (after chlorination)	Not mentioned	Hyperchlorination > 2 ppm; different brands of EFs
			25 brand B	8%†, 8%† (after chlorination)		
Leprat et al.[3]	Hematology ward	Cohort study	3	Not mentioned	100%	Disinfected with chlorine 6 times
Current	Hospital kitchen	Cohort study	27	73%	8%	Control samples from manual faucets did not exceed reference values

EFs = electronic faucets.
*Reference value < 100 colony-forming units (CFU)/mL (European standard).
†Reference value < 500 CFU/mL (U.S. standard).

Two months after the kitchen was opened, 100% of the water samples did not comply with the drinking water regulation (Table 1, period C). The steps taken to eliminate the bacterial contamination were repeated flushing (Table 1, period D), installation of a check valve (period E), chlorination with 0.4 mg/L of chlorine dioxide (period F), and change of faucet aerators (period G). For the chlorination period (period F), the reference value for the bacteria counts at 22°C was 20 CFU/mL according to the German drinking water regulation. Thus, a high percentage were above this reference value. However, it was not possible to eliminate the bacterial contamination in the electronic faucets.

Throughout the study period, all control samples taken from manual faucets in the kitchen complied with the limit and reference values of the German drinking water regulation.

Due to the bacterial growth in the electronic faucets, they were removed completely and replaced with conventional elbow-operated faucets. After that, all water samples complied with the German drinking water regulation.

DISCUSSION

Conventional faucets with handles are rarely reported as a source of bacterial transmission in outbreaks. Mermel et al. reported an outbreak due to *Shigella* in a clinical microbiology laboratory.[5] In a case–control study, they identified contaminated faucet handles as a significant risk factor. After the faucets had been changed to handle-free ones, no further cases occurred. Microbial cross-contamination and potential pathogen spread through faucet handles in hospitals has also been demonstrated by others.[6-8] In areas where contamination occurs through physical contact with faucet handles, conventional manual elbow-operated handles are used (eg, for surgical handwashing and hand scrubbing in operating theaters). Electronic faucets with nontouch technology are an alternative to these manual faucets. When the hands are placed below the outlet in front of the sensor, a jet of water is released. When the hands are removed, the water stops immediately. However, the handling of electronic faucets is often insufficient and they are not always readily accepted. Because the sensor has a delayed reaction, the user often becomes impatient and touches the outlet to initiate the jet of water. Thus, the detection of fecal coliform bacteria in periods A and F was possibly a retrograde contamination.

Due to the water-saving function of the electronic faucets, there was not enough water to sufficiently flush them to clean them. This resulted in the repeated finding of *P. aeruginosa* and other nonfermentative gram-negative bacteria during our examinations and hinted at a rapid growth of biofilm due to the construction of the faucets. In a case–control study by Assadian et al., no significant differences were observed concerning the occurrence of *P. aeruginosa* between electronic faucets and conventional faucets.[9] Unfortunately, no bacteria counts were performed to indicate whether the bacterial contamination in this study exceeded the reference values for a possible bacterial contamination. Halabi et al. revealed these differences in their examinations of electronic faucets with and without temperature selection.[1] Differences between

different manufacturers were described by Hargreaves et al.[2] Table 2 summarizes all published studies about electronic faucets.

In hospital kitchens, electronic faucets are important for preventing cross-contamination through the processing of raw food or through contact with hands. Also, food that is not properly processed through cooking or boiling can be hazardous to patients.

Although electronic faucets were used during the entire period of investigation, it was not known whether kitchen staff, patients, personnel, or students had become ill as a result of eating the food prepared in the kitchen.

During the study period, we did not detect changes in hospital infections due to nonfermentative gram-negative bacteria such as *P. aeruginosa* through our routine infection control surveillance.

As a result of our analysis and other studies, the use of electronic faucets in high-risk areas of hospitals can be considered a potential source for nosocomial pathogens.[1-3] We would not recommend electronic faucets in hospitals. If these devices are to be used in hospitals, water quality should be periodically examined.

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Colonization of Personal Digital Assistants Carried by Healthcare Professionals

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ABSTRACT

This study evaluated personal digital assistant (PDA) microbial colonization before and after cleaning with alcohol. Samples from 75 PDAs were processed. Before cleaning, 96% of the samples were culture positive. After cleaning, 75% became culture negative. PDAs cleaned with an alcohol swab demonstrated significant reduction in colonization (*Infect Control Hosp Epidemiol* 2004;25:1000-1001).

Nosocomial infections are associated with significant mortality and morbidity and have an annual cost of approximately $4.5 billion.[1,2] Healthcare workers are a potential source of nosocomial infections with many pathogens transmitted by hand carriage and contaminated medical devices. Stethoscopes, white coats, gloves, and electronic thermometers have all been shown to harbor potentially pathogenic bacteria and serve as vectors for transmission of infection.[3-8] Personal digital assistants (PDAs) are being increasingly used by healthcare professionals in hospital settings for the management of patients. This study was conducted to assess the colonization rate of PDAs carried by healthcare professionals and to determine the efficacy of a single 70% isopropyl alcohol swab in reducing contamination.

METHODS

A prospective, cross-sectional analysis was conducted from March 1 to May 1, 2004, in a 600-bed, acute care, metropolitan teaching hospital in New York (Long Island Campus of the Albert Einstein College of Medicine). The study was approved by the hospital's institutional research review board. Healthcare workers who regularly used their PDAs in the hospital to provide direct patient care were asked to participate in the study. The investigators made unannounced visits to the hospital floors. The areas visited included the medicine, oncology, and obstetrics and gynecology units; the medical, surgical, and heart–surgical intensive care units; and the emergency department.

With the use of dry, sterile culture swabs (BBL CultureSwab EZ II, Becton Dickinson Microbiology Systems, Cockeysville, MD), samples were taken from the PDA stylus, screen, and margins. The PDA was then cleaned with a single 70% isopropyl alcohol swab (Webcol Alcohol Prep, Kendall Co., Mansfield, MA). The PDA was allowed to dry before additional samples were taken in the same fashion. Swabs were inoculated onto plates containing 5% sheep blood agar (Becton Dickinson Microbiology Systems) within 3 hours of collection and incubated at 35°C for 24 hours. Total colony-forming units were determined by counting colonies on primary plates at 24 hours. Organisms were initially identified by Gram stain, in addition to colony and cell morphologies. Gram-positive organisms were identified to the genus level using standard National Committee for Clinical Laboratory Standards microbiologic methods. *Staphylococcus aureus* and *Enterococcus* isolates were also tested for methicillin and vancomycin resistance, respectively, using standard disk-diffusion methods.[9] Fungal isolates recovered from PDAs were identified on the basis of colony and cell morphologies.

Descriptive statistics are presented as relative fre-

quencies. Differences in the presence or absence of organisms before and after the intervention were determined for the entire sample. Determinations were made for each of the various staff (ie, resident, attending physician, and physician assistant) and for type of service (ie, medical, surgical, emergency department, and obstetrics and gynecology) and were tested for significance using the sign test. All tests of significance were two-tailed with a P value of .05.

RESULTS

Samples were obtained from 75 PDAs of healthcare professionals: 41 internal medicine residents, 11 physician assistants, 10 emergency department residents, 6 medical attending physicians, 4 surgical residents, 2 nurses, and 1 obstetrics and gynecology resident. Seventy (93%) of the participants never cleaned their PDAs. Of the five who cleaned their PDAs, four reported doing so once every 2 to 4 weeks and one did so daily. All participants had been using their PDAs for at least 3 months. Prior to cleaning, 72 (96%) of the PDAs were culture positive. Sixty-four (85%) of the PDA samples grew coagulase-negative *Staphylococcus* (CNS). *S. aureus* was isolated in 8 (11%): 6 (75%) of these were methicillin resistant. Vancomycin-resistant *Enterococcus* (VRE) was isolated from only one PDA (1%). Other bacterial genera isolated were *Bacillus* (17; 23%), *Corynebacterium* (5; 7%), and *Micrococcus* (4; 5%). *Aspergillus* (2; 3%) and *Rhizopus* (1; 1%) were also recovered. No gram-negative organisms were isolated. After cleaning, 54 (75%) of the 72 previously colonized PDAs were found to be culture negative. Twenty-five percent of the cleaned PDAs grew similar organisms, primarily CNS, but with marked reduction in colony-forming units. Overall, PDA colonization with staphylococci was significantly reduced ($P < .0001$). There were no reports of PDA damage due to cleaning with alcohol.

DISCUSSION

Medical instrument colonization as a potential vector for nosocomial infection has been investigated in several studies. The most common organisms isolated were gram-positive cocci, primarily staphylococci. Smith et al. determined that stethoscopes may be important in the spread of infectious agents and recommended that strategies to reduce the contamination be developed.[5] Marinella et al. confirmed this finding in their study, which showed that 100% of stethoscopes were contaminated with CNS and 38% with *S. aureus*.[6] During an investigation of a VRE outbreak, Livornese et al. determined that electronic thermometers were vehicles for VRE transmission.[7] Zachary et al. found a high rate of gown, glove, and stethoscope contamination with VRE.[8] In addition, a study examining the contamination of hospital pagers reported a 21% colonization rate with *S. aureus*, which was reduced by an average of 94% when the pagers were cleaned with an alcohol swab.[10]

During the past few years, PDAs have been increasingly used by healthcare workers. Braddy et al. examined the colonization of PDAs in both hospital and clinic settings. In their study, only 14.6% of the PDAs sampled were used in the healthcare setting and 40% of them were colonized. The most common organism recovered was CNS (82%); none grew methicillin-resistant *S. aureus*, VRE, or gram-negative organisms. Sixty-seven PDAs had not been previously cleaned, and the investigators did not study the efficacy of a cleaning agent.[11]

Our study demonstrated that PDAs used in a hospital setting are colonized with multiple organisms. The use of a 70% isopropyl alcohol swab as a cleaning agent was effective in reducing colonization. Although universal precautions, including handwashing and barrier protection, remain among the most important infection control measures, there has been poor compliance with them in the hospital setting. Infrequent cleaning of medical equipment by healthcare professionals has been documented by several studies and is supported by our data.[4,6,9,10]

To our knowledge, this study is the first to examine both the microbial colonization of PDAs used by healthcare professionals and the efficacy of a single 70% alcohol swab in reducing contamination. PDAs carried by healthcare professionals can harbor pathogenic organisms that may contribute to nosocomial infection. PDAs cleaned with a single 70% isopropyl alcohol swab were found to have a significant reduction in colonization by staphylococci, the most common organism isolated. Although there is no direct evidence to show that microorganisms on PDAs will infect patients, strategies to reduce colonization should be considered.

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Persistent *Acinetobacter baumannii*? Look Inside Your Medical Equipment

A. T. Bernards, PhD; H. I. J. Harinck, PhD; L. Dijkshoorn, PhD; T. J. K. van der Reijden, Ing; P. J. van den Broek, PhD

ABSTRACT

Two outbreaks of multidrug-resistant *Acinetobacter baumannii* occurred in our hospital. The outbreak strains were eventually isolated from respiratory ventilators, an apparatus used to cool or warm patients, and four continuous veno-venous hemofiltration machines. Removing dust from the machines and replacing all dust filters brought the outbreaks to an end (*Infect Control Hosp Epidemiol* 2004;25:1002-1004).

Multidrug-resistant *Acinetobacter baumannii* continues to cause outbreaks in intensive care units (ICUs) around the world.[1-3] The epidemiology of *A. baumannii* is diverse. Outbreaks may originate from a single contaminated source such as ventilators or room humidifiers, the outbreak strain may become widespread with heavy contamination of the environment, or no reservoir may be found.[1-5]

Between October 2000 and July 2003, two outbreaks caused by two distinct strains of multidrug-resistant *A. baumannii* occurred in our university hospital. Both outbreaks occurred in the medical ICU and spread to other ICUs located in different parts of the hospital.

The first outbreak began in October 2000 and was caused by a multidrug-resistant strain of *A. baumannii*. In total, 29 patients were affected, 27 being colonized and 2 having a possible infection (positive blood cultures). All 29 patients were colonized in the respiratory tract. In 17 patients, the respiratory tract was the body site found to be colonized first. Colonized patients were placed in strict isolation (ie, placed in a separate room with an anteroom with negative air pressure). In addition, healthcare workers entering the patients' rooms wore protective clothing, gloves, and a mask at all times. Hygienic measures were intensified (ie, healthcare workers were instructed about strict adherence to hand hygiene between and during bronchial washings, flushing gastric tubes, caring for wounds, and washing of patients). Supplies of utility goods at the patients' bedsides were kept to a minimum. The cleaning of reusable items such as ventilation bags and tubing was improved by placing them appropriately in the washing machine. Hammocks for weighing patients were adequately cleaned and disinfected. Also, the ward was cleaned more frequently, with particular attention paid to areas where dust was likely to gather.

Although environmental cultures showed no contamination of objects on the ward, the medical ICU was at one time closed and cleaned extensively. However, soon after the ward was reopened, the outbreak strain was again isolated from patients. A second investigation into a possible environmental source was begun.

The second outbreak of a multidrug-resistant strain of *A. baumannii* began in May 2003 in the medical ICU. One patient had an infection of a hip prosthesis by *A. baumannii* superimposed on an infection caused by *Staphylococcus aureus*. Three other patients became colonized with the multidrug-resistant strain, two in the respiratory tract and one in the digestive tract. When a patient in the neurosurgery ICU who had not been admitted to the medical ICU became colonized with the same strain in an abdominal wound, an investigation was started. The findings of the investigation of the first outbreak were helpful in tracing the source of the second outbreak quickly.

METHODS

Initially during the first outbreak, 110 environmental objects were sampled including sinks, table tops, computer keyboards, objects on the crash car, ventilation masks, key panels of ventilators, monitors, infusion equipment, hammocks for weighing patients, air conditioner inlets and outlets, and dust. Medical equipment was sampled after it had been cleaned and disinfected according to standard procedures.

Later during the first outbreak, the environmental investigation consisted of sampling a so-called test lung used to check the ventilators before each new patient, a ventilator that was cleaned and disinfected according to standard protocol, and the filters inside the Bair Hugger (Augustine Medical, Inc., Eden Prairie, MN). The ventilator was sampled by opening both the pneumatic and the electronic parts and harvesting the dust from the interior. The interior of the ventilation tubing inside the pneumatic part of the ventilator was not sampled. The Bair Hugger is connected to the patient's mattress by a tube through which cold or warm air is passed to either cool or warm the patient. Several dust filters from the interior of the Bair Hugger were cultured.

Samples for cultures were collected from the surface of the objects with a moistened swab. Dust was collected using moistened swabs. Swabs were then vigorously shaken in 40 mL of acetate mineral medium for enrichment.[6] Filters were cut into small pieces and added to the mineral medium. After 48 hours in a shaking incubator at 30°C, the medium was subcultured onto sheep blood agar and cystine lactose electrolyte deficient agar. Sheep blood sedimentation plates were placed in patients' isolation rooms, on the ward, and in the nurses' station.

Isolates were identified as *Acinetobacter* and susceptibility tests were performed using VITEK 2 (bioMérieux, Hertogenbosch, the Netherlands). Species and strain identification was performed using amplified fragment-length polymorphism (AFLP).

AFLP, previously found to be a useful fingerprinting method,[7] was performed according to Nemec et al.[8] Briefly, purified DNA was digested with *Eco*RI and *Mse*I while ligation of *Eco*RI and *Mse*I adapters was performed. Polymerase chain reaction was performed with a Cy5-labeled *Eco*RI+A primer and a *Mse*I+C primer (A and C representing selective nucleotides). The ALFexpress II DNA analysis system (Amersham Biosciences, Roosendaal, the Netherlands) was used for fragment sep-

aration. Fragments of 50 to 500 bp were subjected to cluster analysis using BioNumerics software (release 2.5; Applied Maths, Sint-Martens-Latem, Belgium) with an overall tolerance setting of 0.1%. The Pearson product moment coefficient (r) was used as a measure of similarity, and the unweighted pair group average linked method was used for grouping.

RESULTS

The initial environmental investigation revealed no contaminated objects. Only one sedimentation plate from a colonized patient's isolation room within 3 m of the patient's bed was positive. During the subsequent environmental investigation of the first outbreak, the outbreak strain was isolated from medical equipment (ie, from dust in the interior of a mechanical ventilator and from filters inside the Bair Hugger). The isolates of the patients and the isolates from the ventilator and the Bair Hugger were resistant to all beta-lactam antibiotics, cotrimoxazole, and the fluoroquinolones. They were intermediately susceptible to meropenem and amikacin, and fully susceptible to tobramycin only. The multidrug-resistant *Acinetobacter* was identified as *A. baumannii* by AFLP because the isolates clustered with the reference strain of *A. baumannii* 50% or more. The AFLP profiles of patient and environmental isolates clustered well above 90%, indicating that they belonged to the same strain (Figure). After removal of the dust from the interior of the ventilator by forced air, the outbreak strain was no longer isolated from the machine.

The second outbreak was caused by an *Acinetobacter* resistant to all beta-lactam agents tested, the fluoroquinolones, and the aminoglycosides. The isolate was susceptible to meropenem only.

Different ventilators had been used for the affected patients. The only pieces of equipment that had been used by all colonized patients except one were the continuous veno-venous hemofiltration (CVVH) machines. During the 2-month period from the day of admission of the index patient to the day the CVVH machines were sampled, 175 patients were admitted to the medical ICU and the neurosurgery ICU. Eleven of these 175 patients received CVVH. The outbreak strain was isolated from 3 (27%) of the 11 patients, and 2 (1%) of 164 patients not receiving CVVH were found to harbor the outbreak strain. Thus, patients who had the outbreak strain were more likely to have received CVVH (odds ratio, 30.4; 95% confidence interval, 6 to 146). The outbreak strain was isolated from dust inside both the blood compartment and the substitution compartment of 4 of the 6 machines present in our hospital. The isolates of both patients and CVVH machines were identified as *A. baumannii* and appeared to represent the same strain on AFLP analysis (Figure). After removal of the dust from the interior of all CVVH machines, the outbreak strain was no longer isolated from any of the machines or patients.

DISCUSSION

Bacteria belonging to the genus *Acinetobacter* are known to be capable of surviving in dry conditions.[9,10]

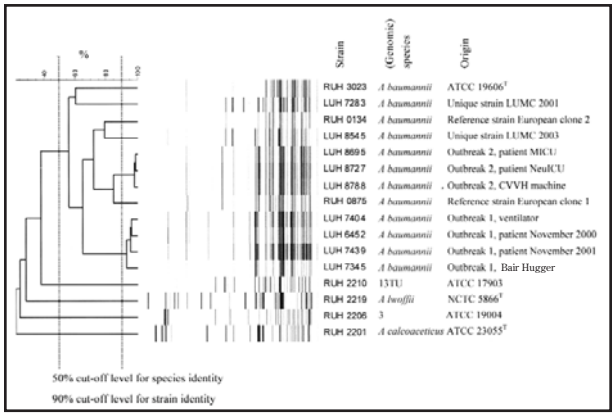

FIGURE. Amplified fragment-length polymorphism fingerprints of patients' isolates, of isolates from medical equipment of the first outbreak (outbreak 1) and the second outbreak (outbreak 2), and of reference strains of five *Acinetobacter* species, including *A. baumannii*. Levels of similarity are expressed as percentages of similarity. RUH = Rotterdam University Hospital; LUH = Leiden University Hospital; LUMC = Leiden University Medical Center; MICU = medical intensive care unit; NeuICU = neurosurgery ICU; CVVH = continuous veno-venous hemofiltration; ATCC = American Type Culture Collection; NCTC = National Collection of Type Cultures.

Dust contaminated with *A. baumannii* may thus be a relevant vehicle in the transmission of this bacterium.

In our 882-bed, tertiary-care hospital, *A. baumannii* is not a frequent occurrence. The numbers of patients from whom *A. baumannii* was isolated from 1999 through 2002 were 5, 23, 29, and 5, respectively, with incidences of 0.03, 0.07, 0.06, and 0.03 per 1,000 patient-days, respectively. Ten of the 23 *A. baumannii* isolates in 2000 and 19 of the 29 in 2001 were the outbreak strain and occurred in the ICUs only.

In the first outbreak, the strain involved was found in the interior of a ventilator and of the Bair Hugger. After removal of the dust inside all ventilators and replacement of the filters of the Bair Hugger, the outbreak strain was no longer isolated from patients. In the second outbreak, the strain involved was isolated from dust inside the CVVH machines, which had been used on all colonized patients except one. After removal of the dust from the CVVH machines using forced air, the outbreak strain was no longer isolated.

During operation, a fan provides continuous airflow through ventilators and CVVH machines to cool the circuit boards. It is possible that dust carrying bacteria is passed in and out of the machines on this air current, despite dust filters being placed at the air inlets and outlets. The Bair Hugger is designed to create an airflow; dust is sucked into the machine, with filters becoming contaminated and possibly serving as a secondary source of transmission. It was not known how long the filters had been in place, and there was no protocol for regular replacement of the filters. We believe the outbreak strain was transmitted by being carried on contaminated dust from within the machines to the exterior during operation when a fan created an air current. Thus, the exterior of

the machines may have been contaminated and become a secondary source of spread.

We found contaminated dust in the interior of different types of machines used by patients on two different occasions. After this dust was removed, no further cases were observed. Hence, dust may be relevant in the epidemiology of *A. baumannii* or of any microorganism capable of surviving under dry conditions. We recommend that during outbreaks of *A. baumannii* the removal of dust from the interior of machines that patients come in close contact with be an integral part of cleaning and disinfection procedures.

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Epidemiologic Study of Nosocomial Urinary Tract Infections in Saudi Military Hospitals

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ABSTRACT

A case–control study of patients with and without confirmed UTI was performed to identify risk factors for nosocomial UTI. Duration of hospitalization, unit of admission, history of diabetes mellitus or debilitating diseases, and duration and number of urinary catheters were independently associated with increased risk of nosocomial UTIs (*Infect Control Hosp Epidemiol* 2004;25:1004-1007).

In developing countries, nosocomial infection is increasingly being recognized as a significant problem. Nosocomial infection often results in extended hospitalization, expensive therapy, and morbidity and mortality.[1,2] Up to 10% of all hospitalized patients develop nosocomial infection.[3,4] Urinary tract infections (UTIs) are the most common type of nosocomial infection, accounting for 40% of all infections in hospitals and 34% of all infections in nursing homes.[5,6] In hospitals, 80% to 90% of nosocomial UTIs are associated with the use of urinary catheters and an additional 5% to 10% are associated with other genitourinary manipulations.[6-8] Prevention and management of such infections require an intimate knowledge of their epidemiology, including risk factors.[9,10] Hospital infection control programs can prevent 33% of nosocomial infections, including nosocomial UTIs.[11] The aims of this study were to estimate the overall rates of nosocomial infections and nosocomial UTIs and their linear trends during 5 years (1998 to 2002) and to identify potential risk factors of hospitalized patients who developed nosocomial UTIs.

METHODS

To fulfill the objectives of this study, two methodologies were adopted: a case–control study of risk factors and a record review to calculate nosocomial UTI rates.

The case–control study of risk factors was performed between August 1, 2001, and July 31, 2003, at Al-Hada (400 beds), Al-Rehab (100 beds), and Prince Sultan (50 beds) military hospitals. These three hospitals are administered by the Medical Service Department of the Saudi Arabian Ministry of Defense and Aviation. All patients admitted to these hospitals for at least 72 hours during the study period were considered eligible for inclusion in the study. Among these, patients proved to have UTI were considered case-patients. The diagnosis of UTI was made according to criteria of the Centers for Disease Control and Prevention.[12] After exclusion of patients who did not fulfill eligibility criteria, three control-patients were enrolled for each case-patient through a systematic random sampling procedure using the patient admission record list (every three patients).

For all participants (case-patients and control-patients), the following were recorded: age, gender, unit of admission, presence of a catheter, duration of catheterization, number of catheters, history of diabetes mellitus, history of immunosuppressive drug use, history of debilitating diseases (cancer, liver failure, or uremia), and duration of hospitalization. These data were collected from the patients' records during their hospital stay by a trained nosocomial infection surveillance team from the Preventive Medicine Department.

Hospital records, providing the number of patients hospitalized each month and the numbers of nosocomial infections (crude and site specific) each month, were reviewed. The overall annual rates of nosocomial infections and nosocomial UTIs during the period 1998 to 2002 were calculated by dividing the total number of nosocomial infections (crude and UTIs) pooled throughout all

TABLE 1
BASELINE CHARACTERISTICS OF PARTICIPANTS IN THE CASE–CONTROL STUDY

Characteristic	No. of Case-Patients (n = 206)	No. of Control-Patients (n = 618)	Total No. (N = 824)
Age, y*			
⩽ 15	33 (16.1%)	136 (22.0%)	169 (20.5%)
> 15 to 45	53 (25.7%)	152 (24.6%)	205 (24.9%)
> 45 to 65	40 (19.4%)	143 (23.1%)	183 (22.2%)
> 65	80 (38.8%)	187 (30.3%)	267 (32.4%)
Mean	46.8	43.7	44.8
SD	29.3	29.4	29.6
Median	50.0	47.0	47.0
Range	2 d to 95 y	2 d to 87 y	2 d to 95 y
Gender†			
Male	104 (50.5%)	330 (53.4%)	434 (52.7%)
Female	102 (49.5%)	288 (46.6%)	390 (47.3%)

SD = standard deviation.
*P = 064.
†P = .381.

TABLE 2
RISK FACTORS ON MULTIVARIATE ANALYSIS*

Risk Factor	Adjusted OR	CI_{95}
Duration of hospitalization, wk		
< 1†	1.0	
1 to 3	1.06	0.68–2.14
> 3	2.18	1.24–3.29‡
Unit of admission		
Medical ICU†	1.0	
Surgical ICU	1.91	0.96–4.01
Nursery ICU	2.73	1.68–4.01‡
Burn ICU	3.05	1.74–4.13‡
Other	1.16	
No. of urinary catheters		
None†	1.0	
1	1.99	0.92–3.72
2	2.18	1.22–5.14‡
> 2	4.56	2.04–6.28‡
Duration of catheterization, d		
⩽ 3†	1.0	
> 3	3.01	1.87–6.21‡
Diabetes mellitus		
No†	1.0	
Yes	6.27	2.22–9.52‡
Underlying debilitating disease§		
No†	1.0	
Yes	3.11	1.29–8.18‡

OR = odds ratio; CI_{95} = 95% confidence interval; ICU = intensive care unit.
*Age and history of immunosuppressive drug use were removed from the final model.
†Reference category.
‡P < .05.
§Cancer, liver failure, or uremia.

months by the total number of patients hospitalized multiplied by 100. Critically ill patients (those admitted to the medical intensive care unit [ICU], surgical ICU, nursery ICU, or burn ICU) were treated as a separate group. Overall and UTI rates were calculated for this particular group.

Statistical analysis was performed with SPSS software (version 10.0; SPSS, Inc., Chicago, IL). A linear trend was applied to search for evidence of a change in the overall incidence of nosocomial infections and UTIs over time. Age, gender, duration of hospitalization, unit of admission, number of urinary catheters, duration of catheterization, history of diabetes mellitus, history of underlying debilitating diseases, and history of immunosuppressive drug use were treated as categorical variables. The crude measure of association between single putative risk factors and nosocomial UTIs was expressed as an odds ratio (OR) with a 95% confidence interval (CI_{95}). Multiple associations were evaluated in multiple logistic regression models using backward stepwise selection. This process allowed estimation of the strength of the association between each independent variable and the dependent variable taking into account the potential confounding effects of the other independent variables. The covariates were removed from the model if the likelihood estimates had a P value of greater than .10. Each category of predictor variables was contrasted with the initial category (reference category). An adjusted OR with a CI_{95} that did not include 1.0 was considered significant.

RESULTS

A total of 206 discharged patients with nosocomial UTI and 618 control-patients without nosocomial UTI were recruited. Their baseline characteristics (age and gender) are presented in Table 1. The ages of the case-patients ranged from 2 days to 95 years (mean, 46.8 ± 29.3 years; median, 50.0 years), whereas the ages of the control-patients ranged from 2 days to 87 years (mean, 43.7 ± 29.4 years; median, 47.0 years). The difference between the two groups was not statistically significant (P = .064). Females represent 49.5% and 46.6% of case-patients and control-patients, respectively. There was no significant difference between the groups in this regard (P = .381).

The results of logistic regression analysis of the risk factors examined for nosocomial UTIs are summarized in Table 2. Nosocomial UTIs were significantly associated with being hospitalized for more than 3 weeks compared with less than 1 week (OR, 2.18; CI_{95}, 1.24 to 3.29). Regarding unit of admission, patients admitted to the ICUs (OR, 2.73; CI_{95}, 1.68 to 4.01) were more likely to develop nosocomial UTI than were those admitted to medical units (OR, 3.05; CI_{95}, 1.74 to 4.13). Number of urinary catheters and duration of catheterization were associated with the outcome of interest. Patients with two urinary catheters (OR, 2.18; CI_{95}, 1.22 to 5.14) and those with

TABLE 3
DISTRIBUTION OF TOTAL DISCHARGED PATIENTS ACCORDING TO THE PRESENCE OF NOSOCOMIAL INFECTION AND NOSOCOMIAL URINARY TRACT INFECTION DURING 1998 TO 2002

Year	Total No. of Discharged Patients	No. of Patients With Nosocomial Infection (%)	No. of Patients With Nosocomial UTI (%)	Nosocomial UTI/Total Nosocomial Infection Rate
1998	10,967	285 (2.60)	86 (0.78)	30.18
1999	14,391	298 (2.07)	98 (0.68)	32.89
2000	10,672	373 (3.50)	108 (1.01)	28.95
2001	9,114	274 (3.01)	88 (0.97)	32.12
2002	9,782	224 (2.90)	77 (0.79)	34.38

UTI = urinary tract infection.

TABLE 4
DISTRIBUTION OF DISCHARGED CRITICALLY ILL PATIENTS* ACCORDING TO THE PRESENCE OF NOSOCOMIAL INFECTION AND NOSOCOMIAL URINARY TRACT INFECTION DURING 1998 TO 2002

Year	Total No. of Discharged Critically Ill Patients	No. of Patients With Nosocomial Infection (%)	No. of Patients With Nosocomial UTI (%)	Nosocomial UTI/Total Nosocomial Infection Rate
1998	691	82 (11.9)	31 (4.5)	37.80
1999	901	106 (11.8)	39 (4.3)	36.79
2000	686	81 (11.8)	29 (4.2)	35.80
2001	572	69 (12.1)	21 (3.7)	30.43
2002	620	78 (12.6)	26 (4.2)	33.33

UTI = urinary tract infection.
*Those admitted to the medical intensive care unit (ICU), surgical ICU, nursery ICU, or burn ICU.

more than two urinary catheters (OR, 4.56; CI_{95}, 2.04 to 6.28) had an increased risk of nosocomial UTI compared with patients with no history of urinary catheters. Patients catheterized for more than 3 days had a 3-fold risk of UTI compared with those catheterized for 3 days or less (OR, 3.01; CI_{95}, 1.87 to 6.21). Diabetes mellitus was strongly and positively related to nosocomial UTI (OR, 6.27; CI_{95}, 2.22 to 9.52). The presence of an underlying debilitating disease was also significantly associated with an increased risk of nosocomial UTI (OR, 3.11; CI_{95}, 1.29 to 8.18).

The overall incidence of nosocomial infection during the study period ranged from 2.07 to 3.50 per 100 discharged patients (mean, 2.82). The overall incidence of nosocomial UTI ranged from 0.68 to 1.01 per 100 discharged patients (mean, 0.85). UTIs represented 31.7% of all nosocomial infections throughout the study period (Table 3). For critically ill patients, who were a separate group, the mean overall incidence rates of nosocomial infection and nosocomial UTI were 12.04 and 3.45 per 100 patients, respectively, throughout the study period. UTIs represented approximately one-third of all nosocomial infections (34.83%) among ICU patients (Table 4).

DISCUSSION

Hospital-acquired UTIs usually cause mild to moderate adverse effects, but sometimes worsen. The risk of acquiring a UTI depends on the method and duration of catheterization, the quality of catheter care, and host susceptibility.[13] In one study, UTIs were identified in approximately 30% of patients with urinary catheters within 2 weeks and in virtually 100% at 6 weeks.[14] The current study revealed that the number of catheter insertions and the duration of catheterization play a significant role in determining the occurrence of nosocomial UTI.

The highest rates of nosocomial UTI were observed in ICUs, where the most severely ill patients were treated and the highest mortality rates were seen. Similar findings have been previously reported.[15] Our findings are in agreement with other studies reporting that there is a greater risk for nosocomial UTI with increased duration of catheterization.[16]

Females were not at a higher risk for nosocomial UTI in the current study. This is in contrast to what other controlled studies have reported.[17]

Duration of hospitalization was a strong predictor of outcome as in another recent study.[17]

Diabetes mellitus was a significant risk factor for UTI. In a study conducted by de-Aguia et al.,[18] UTI was the most frequent infection among patients with diabetes.

In our study, UTIs accounted for approximately one-third of all nosocomial infections, which is slightly lower than what others have reported.[5,6] The overall rates of nosocomial infection and nosocomial UTI remained remarkably stable throughout the study period. Studies in recent decades have suggested that the attack rate of nosocomial UTI may be decreasing,[19] perhaps due to shorter periods of catheter use, more attention to catheter hygiene, increased antibiotic use, or all three.

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